DAIDS
Bethesda, MD USA

POLICY

Requirements for DAIDS Funded and /or Sponsored Laboratories in Clinical Trials

Approval Date: 15 APR 09 No.: DWD-POL-LB-005.03
Effective Date: 15 MAY 09

NOTE: This Policy has been reviewed for accuracy and updated to meet 508 compliance guidelines. DAIDS has identified five specific requirements for laboratory performance as opposed to six listed in the previous version of the policy and requires laboratories to have documented Quality Management Plans (QMP). Key changes also include the removal of Research Use Only (RUO) Tests and the addition of Non FDA approved End Point tests listed in section 6.2.2. This version supersedes version 2.0 dated 20 DEC 06.

1.0 PURPOSE

The Division of Acquired Immunodeficiency Syndrome (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID) has established specific requirements for laboratories processing and testing biologic samples from participants enrolled in clinical trials funded and/or sponsored by DAIDS. These requirements relate to general laboratory operations, quality assurance and control procedures, management of specimens, and management of laboratory data. The purpose of this policy is to safeguard participants enrolled in clinical trials and to ensure the reliability and validity of all laboratory measurements taken to determine eligibility, identify and manage adverse events, and assess outcomes during the course of the clinical trial.

2.0 SCOPE

This policy applies to all laboratory procedures in support of a therapeutic, vaccine, or prevention clinical trial funded and/or sponsored by DAIDS.

3.0 BACKGROUND

This policy identifies requirements regarding laboratory operations in order to ensure compliance of laboratories with the Code of Federal Regulations (CFR) and the DAIDS Guidelines for Good Clinical Laboratory Practice (GCLP) Standards. The GCLP concept possesses a unique quality, as it embraces both the research/pre-clinical and clinical aspects of Good Laboratory Practice (GLP). GCLP standards encompass applicable portions of 21 CFR part 58 (or GLP), 42 CFR part 493 (or Clinical Laboratory Improvement Amendment -CLIA), and they are enhanced by standards from accrediting bodies such as the College of American Pathologists (CAP) and South African National Accreditation System . The purpose of these regulations is to promote good laboratory practices and to assure reliable laboratory results and documentation/records. Regulations under these guidelines define requirements for personnel, procedures, and policies.

4.0 DEFINITIONS

For additional definitions see DAIDS glossary.

http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/Glossary.htm

5.0 RESPONSIBILITIES

This policy, and the associated specific requirements for U.S. and non-U.S. laboratories has been created by DAIDS staff whose responsibility is to oversee the laboratory component of DAIDS funded and /or sponsored clinical trials. DAIDS staff will be responsible for updating this standard in response to changes in federal regulations and based on continued experience in the conduct of clinical trials. DAIDS staff will be responsive to queries by investigators who need assistance with understanding this policy and with implementing the specific requirements for U.S. and non-U.S. laboratories. The Principal Investigator is responsible for ensuring that laboratories processing and testing biologic samples from participants enrolled in clinical trials adhere to the laboratory requirements identified in this policy. The lab manager is responsible for the day-to-day operations of the laboratory and for ensuring that the requirements of this policy are met.

6.0 POLICY

6.1. All NIH/NIAID/DAIDS-supported clinical trials involving human subjects must ensure compliance with federal regulations including procedures to protect the safety of all participants. These studies must be conducted in a manner to assure the sponsor and regulatory agencies that all data submitted are a true reflection of the results obtained during a study and that this data can be relied upon when making risk and/or safety assessments of study products. DAIDS has determined that Good Clinical Laboratory Practices (GCLP) are the minimal requirements that clinical research laboratories should follow (see Appendix 3).

6.2. In addition to maintaining operations in compliance with GCLP, DAIDS has established and maintains specific requirements for laboratory performance in five areas.

6.2.1. Diagnostics, Safety Tests, CD4, Virological and Pharmacological Tests

Tests that are used for diagnosis, determining eligibility, endpoints, monitoring the safety of the intervention and making patient

management decisions must be performed in laboratories that conduct operations in accordance with GCLP. These tests must be quality assured by external proficiency testing surveys. When not available, alternative external quality assurance measures should be devised. U.S. laboratories must be CLIA-certified.

6.2.2. Non-FDA Approved End Point Tests

This section covers all research tests not yet approved by the US FDA and validated by International Conference on Harmonisation (ICH) or US Pharmacopeia. The endpoint tests must be performed in laboratories that conduct operations in accordance with GCLP. External quality assurance should be applied to Research Use Only tests. If existing EQA surveys are not available, a suitable form of alternative proficiency assessments should be devised and proposed to DAIDS for approval.

6.2.3. Study Specimen Management

Procedures for the management of trial specimens must be documented and followed to ensure the integrity of specimens and their timely testing. Procedures must address specimen acquisition, receipt, processing, testing, storage and shipping according to regulations (e.g. International Air Transport Association (IATA)) and under conditions that preserve specimen integrity (e.g. maintaining the cold chain), and tracking as applicable.

6.2.4. Study Laboratory Data Management

Procedures for the management of laboratory data must be documented and followed to ensure data integrity and timely reporting of results and are required to include appropriate procedures for data quality assurance (QA) and corrective actions. Procedures should address data acquisition, recording/entry, data modification, signatures, export, archiving and security, as well as integration of the laboratory data with the main study database. Computerized laboratory systems should be validated, taking into account the elements of 21 CFR Part 11 compliance.

6.2.5. Laboratory Quality Management Plan

Laboratories must have a documented Quality Management Plan (QMP) as described in the NIH/NIAID/DAIDS Guidelines for

GCLP Standards to regularly review all components of laboratory activities, including intervention and corrective action plan, and plans for backup testing facilities. All labs must designate a QA manager to be responsible for executing the lab QMP.

These laboratory requirements are reviewed periodically and updated as necessary to maintain currency with accepted practices and technological innovation. For the convenience of current and potential investigators and collaborating laboratories, separate documents with specific requirements are provided for U.S. based laboratories (Appendix 1) and non-U.S. laboratories (Appendix 2). Differences in these documents pertain largely to laboratory accreditation bodies and procedures within and outside of the United States.

6.3. Laboratory Audits

DAIDS and/or its contractors may conduct laboratory-specific audit visits to determine GCLP compliance, laboratory readiness to participate in trials, and, as indicated, during the conduct of a trial.

6.4. Comprehensive laboratory Plan

Applications in response to PAR-05-113 'NIAID Clinical Trial Implementation (U01) Cooperative Agreement' must include a Comprehensive Laboratory Plan in the Appendices 1 and 2 that identifies all proposed laboratories and plans to ensure they meet DAIDS requirements. The required content and suggested formats for the components of the comprehensive Laboratory Plan are detailed in the above referenced documents.

7.0 REFERENCES

U.S. Code of Federal Regulations, Title 21, Parts 11 and 58
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm

U.S. Code of Federal Regulations, Title 42 CFR Part 493
http://www.phppo.cdc.gov/clia/pdf/CMS-2226-F.pdf

CLIA Program – Clinical Laboratory Improvement Amendments
http://www.cms.hhs.gov/clia/

Department of Health and Human Services (DHHS)/Centers for Disease Control and Prevention (CDC) Presentation
http://www.phppo.cdc.gov/dls/ila/cd/botswana/Presentations/QS%20-%20Overview.ppt

Morbidity and Mortality Weekly Report (MMWR) 1997; 46 No. RR-2 Dual-platform technology http://www.cdc.gov/mmwr/preview/mmwrhtml/00045580.htm

MMWR 2003; 52(RR-02) Single-platform technology
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5202a1.htm

International Air Transport Association (IATA) Dangerous Goods Shipping Regulations
http://www.iata.org/ps/publications/9065.htm

Questions and comments regarding this policy may be directed to the OPCRO Policy Group at: NIAIDOPCROPOLICYGROUP@mail.nih.gov

8.0 INQUIRIES

Questions and comments regarding this policy may be directed to the OPCRO Policy Group at: NIAIDOPCROPOLICYGROUP@mail.nih.gov

9.0 AVAILABILITY

This policy is available electronically at the following URL: http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/Default.htm

10.0 CHANGE SUMMARY

This policy supersedes version 2.0 dated 20 Dec 06.

11.0 APPENDICIES

Appendix 1 - DAIDS Requirements for U.S. Laboratories [LB.401]

Appendix 2 - DAIDS Requirements for non-U.S. Laboratories [LB.402]

Appendix 3 - DAIDS Guidelines for Good Clinical Laboratory Practice Standards [LB.403]

12.0 APPROVAL

/Richard Hafner, MD/
Richard Hafner